Amendments to the Claims

1. (Currently Amended) A screening method for the identification of agents which modulate, either directly or indirectly, the interaction of a first polypeptide encoded by a nucleic acid molecule selected from the group consisting of:

a) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 1 or 2 ~~Figure 17a or 17b~~;

b) a polypeptide encoded by a nucleic acid molecule which hybridises to the nucleic acid molecule in (a) and which enhances the pro-apoptotic activity of p53;

c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (a) and (b); with a second polypeptide selected from the group consisting of:

d) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 5, 7, 9, or 11 ~~Figure 18a, 18c, 18e or 18g~~;

e) a polypeptide encoded by a nucleic acid molecule which ~~hybridises~~ hybridizes to the nucleic acid molecule in (d) ~~above~~ and which has the activity associated with Ras or a variant Ras polypeptide;

f) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (d) and (e); the method comprising,

i) forming a preparation comprising said first and second polypeptide;

ii) adding at least one candidate agent to be tested; and

iii) determining the effect, or not, of said agent on the interaction of said first polypeptide with said second polypeptide.

2. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 1 wherein said first polypeptide is represented by the amino acid sequence as shown in SEQ ID NO: 3 or 4 ~~Figure 17c or 17d~~, or a variant polypeptide wherein said variant polypeptide sequence has been altered by addition, substitution or deletion of at least one amino acid residue.

3. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 1 ~~or 2~~ wherein said first polypeptide comprises the amino acid sequence + 1 to +120 of the sequence shown in SEQ ID NO: 2 or 3~~Fig 17c and 17d~~.

4. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 3 wherein said polypeptide consists of the amino acid sequence +1 to +120 of the sequence shown in SEQ ID NO: 3 or 4 ~~Figure 17c or 17d~~.

5. (Currently Amended) [[A]] The method ~~according to any~~ of ~~Claims~~ claim 1[[-4]] wherein said second polypeptide is represented by the amino acid sequence shown in SEQ ID NO: 6, 8, 10, or 12 ~~Figure 18b, 18d, 18f or 18h~~, or a variant polypeptide wherein said variant polypeptide sequence has been altered by addition, substitution or deletion of at least one amino acid residue.

6. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 5 wherein said second polypeptide comprises the amino acid sequence as shown in SEQ ID NO: 8 ~~Figure 18d~~.

7. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 5 ~~or 6~~ wherein said second polypeptide comprises the amino acid sequence as shown in SEQ ID NO: 12~~Figure 18h~~.

8. (Currently Amended) [[A]] The method ~~according to any~~ of ~~Claims~~ claim 1[[-4]] wherein said second polypeptide is modified at amino acid residue 17.

9. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 8 wherein said modification is the substitution of a serine amino acid for an asparagine amino acid.

10. (Currently Amended) [[A]] The method ~~according to any~~ of ~~Claims~~ claim 1[[-9]] wherein said first and second polypeptides are expressed by a cell.

11. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 10 wherein said cell is a cell transfected with at least one nucleic acid molecule(s) which encodes said first and second polypeptides.

12. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 10 ~~or 11~~ wherein the expression of said nucleic acid molecule(s) is regulatable.

13. (Currently Amended) [[A]] The method ~~according to any~~ of ~~Claims~~ claim 10[[-12]] wherein said cell is a cancer cell.

14. (Currently Amended) [[A]] The method ~~according to any~~ of ~~Claims~~ claim 10[[-13]] wherein said cell is part of a transgenic animal wherein the genome of said animal has been modified to include nucleic acid molecules which encode first and second polypeptides.

15. (Currently Amended) [[A]] The method ~~according to any~~ of ~~Claims~~ claim 10[[-14]] wherein said nucleic acid molecules are expressed in a specific cell/tissue.

16. (Currently Amended) A screening method for the identification of agents which modulate, either directly or indirectly, the phosphorylation of a first polypeptide encoded by a nucleic acid molecule selected from the group consisting of:

a) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 1 or 2 ~~Figure 17a or 17b~~;

b) a polypeptide encoded by a nucleic acid molecule which hybridises to the nucleic acid molecule in (a) and which enhances the pro-apoptotic activity of p53;

c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (a) and (b); with a second polypeptide selected from the group consisting of:

d) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 13 or 15 ~~Figure 19a or 20a~~;

e) a polypeptide encoded by a nucleic acid molecule which ~~hybridises~~ hybridizes to the nucleic acid molecule in (d) ~~above~~ and which has protein kinase activity;

f) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (d) and (e); comprising,

i) forming a preparation comprising said first and second polypeptide;

ii) adding at least one candidate agent to be tested; and

iii) determining the effect, or not, of said agent on the phosphorylation state of said first polypeptide.

17. (Currently Amended) A screening method for the identification of agents which modulate, either directly or indirectly, the phosphorylation state of a first polypeptide encoded by a nucleic acid molecule selected from the group consisting of:

a) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 1 or 2 ~~Figure 17a or 17b~~;

b) a polypeptide encoded by a nucleic acid molecule which hybridises to the nucleic acid molecule in (a) and which enhances the pro-apoptotic activity of p53;

c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (a) and (b); with a second polypeptide selected from the group consisting of:

d) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 17 ~~Figure 21a~~;

e) a polypeptide encoded by a nucleic acid molecule which ~~hybridises~~ hybridizes to the nucleic acid molecule in (d) ~~above~~ and which has protein phosphatase activity;

f) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (d) and (e); the method comprising,

i) forming a preparation comprising said first and second polypeptide;

ii) adding at least one candidate agent to be tested; and

iii) determining the effect, or not, of said agent on the phosphorylation state of said first polypeptide.

18. (Currently Amended) [[A]] The method ~~according to any of Claims~~ claim 1[[-17]] wherein said agent is a polypeptide, peptide, or aptamer.

19. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 18 wherein said polypeptide is an antibody, or active binding fragment thereof.

20. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 19 wherein said antibody or binding fragment is a monoclonal antibody.

21. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 19 ~~or 20~~ wherein said ~~antibody~~ active binding fragment is a single chain antibody variable region fragment or a domain antibody fragment.

22. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 19 ~~or 20~~ wherein said antibody is a humanised or chimeric antibody.

23. – 24. (Canceled)

25. (Currently Amended) A ~~cell~~ transfected cell ~~with at least one nucleic acid molecule~~ wherein the genome of said cell is modified to consist of ~~include~~ at least one copy of a nucleic acid molecule encoding a polypeptide ~~selected from the group consisting of:~~

~~a) a polypeptide encoded by a nucleic acid molecule~~ comprising a nucleic acid sequence as represented in SEQ ID NO: 1 or 2 ~~Figure 17a or 17b~~;

~~b) a polypeptide encoded by a nucleic acid molecule which hybridises to the nucleic acid molecule in (a) and which enhances the pro-apoptotic activity of p53;~~

~~c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid~~

~~sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (a) and (b);~~ and at least one copy of a nucleic acid molecule encoding a polypeptide selected from the group consisting of:

~~d)~~ (a) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 5, 7, 9, or 11~~Figure 18a, 18c, 18e or 18g~~;

~~e)~~ (b) a polypeptide encoded by a nucleic acid molecule which ~~hybridises~~ hybridizes to the nucleic acid molecule in (a) ~~(d) above~~ and which has the activity associated with Ras or a variant Ras polypeptide;

~~f)~~ (c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in ~~(d)~~ (a) and ~~(e)~~ (b) wherein said cell is adapted for the regulated expression of said nucleic acid molecule(s).

26. (Currently Amended) A cell transfected with at least one nucleic acid molecule wherein the genome of said cell is modified to include at least one copy of a nucleic acid molecule encoding a polypeptide selected from the group consisting of:

a) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 1 or 2~~ Figure 17a or 17b~~;

b) a polypeptide encoded by a nucleic acid molecule which hybridises to the nucleic acid molecule in (a) and which enhances the pro-apoptotic activity of p53;

c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (a) and (b) and at least one copy of a nucleic acid molecule encoding a polypeptide selected from the group consisting of;

d) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 13 or 15~~Figure 19a or 20a~~;

e) a polypeptide encoded by a nucleic acid molecule which ~~hybridises~~ hybridizes to the nucleic acid molecule in (d) ~~above~~ and which has protein kinase activity;

f) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (d) and (e) wherein said cell is adapted for the regulated expression of said nucleic acid molecule(s).

27. (Currently Amended) A ~~cell~~ transfected cell ~~with at least one nucleic acid molecule~~ wherein the genome of said cell is modified to consist of ~~include~~ at least one copy of a nucleic acid molecule encoding a polypeptide ~~selected from the group consisting of:~~

~~a) a polypeptide encoded by a nucleic acid molecule~~ comprising a nucleic acid sequence as represented in SEQ ID NO: 1 or 2 ~~Figure 17a or 17b~~;

~~b) a polypeptide encoded by a nucleic acid molecule which hybridises to the nucleic acid molecule in (a) and which enhances the pro-apoptotic activity of p53;~~

~~c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (a) and (b)~~ and at least one copy of a nucleic acid molecule encoding a polypeptide selected from the group consisting of;

~~d)~~ (a) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 17 ~~Figure 21a~~;

~~e)~~ (b) a polypeptide encoded by a nucleic acid molecule which ~~hybridises~~ hybridizes to the nucleic acid molecule in (a) ~~(d) above~~ and which has protein phosphatase activity;

~~f)~~ (c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined inv(a) ~~(d)~~ and (b) ~~(e)~~ wherein said cell is adapted for the regulated expression of said nucleic acid molecule(s).

28. (Currently Amended) [[A]] The cell ~~according to any~~ of ~~Claims~~ claim 25[[-27]] wherein said cell further comprises a nucleic acid molecule which includes a reporter gene to monitor the activity of said pro-apoptotic polypeptide(s).

29. (Currently Amended) [[A]] The cell according to any of ~~Claims~~ claim 25[[-28]] wherein said cell is a cancer cell.

30. (Currently Amended) A non-human transgenic animal comprising at least one cell ~~according to any~~ of ~~Claims~~ claim 25[[-29]].

31. (Currently Amended) [[An]] The animal according to ~~Claim~~ claim 30 wherein said non-human animal is a non-human primate.

32. (Currently Amended) [[An]] The animal according to ~~Claim~~ claim 30 wherein said transgenic animal is a rodent or a pig.

33. -34 . (Canceled)

35. (Currently Amended) A ~~combined~~ preparation comprising a nucleic acid molecule which encodes a p53 polypeptide, or sequence variant thereof, and at least one nucleic acid molecule which encodes at least one polypeptide, or sequence variant thereof, as represented by the amino acid sequences shown in SEQ ID NO: 3 or 4, wherein said polypeptides are encoded by a single nucleic acid molecule which is part of a vector and said nucleic acid molecules are operably linked to at least one promoter that controls expression of said nucleic acid molecules~~Figure 17c and/or Figure 17d~~.

36. – 38. (Canceled)

39. (Currently Amended) A method to treat a condition which would benefit from an increase in apoptosis comprising administering a preparation comprising a first nucleic acid molecule comprising a nucleic acid sequence which encodes a p53 polypeptide, or sequence variant thereof, and administering a second preparation comprising a second nucleic acid molecule comprising a nucleic acid sequence which encodes a polypeptide, or sequence variant thereof, as represented by the amino acid sequence as shown in SEQ ID NO: 3 or 4~~Figure 17c and/or Figure 17d~~ wherein said preparations are administered simultaneously, sequentially or delayed manner.

40. (Currently Amended) A method to treat a condition which would benefit from a stimulation of apoptosis comprising administering ~~a combined~~ the preparation of claim 35~~according to any of Claims 34-38~~.

41. (Currently Amended) [[A]] The method according to ~~Claim~~ claim 39 ~~or 40~~ wherein said condition is cancer.

42. (Currently Amended) An antibody, or active binding fragment thereof, wherein said antibody or fragment, specifically binds a polypeptide encoded by a nucleic acid molecule selected from the group consisting of:

a) a polypeptide encoded by a nucleic acid molecule comprising a nucleic acid sequence as represented in SEQ ID NO: 1 or 2~~Figure 17a or 17b~~;

b) a polypeptide encoded by a nucleic acid molecule which ~~hybridises~~ hybridizes to the nucleic acid molecule in (a) and which enhances the pro-apoptotic activity of p53;

c) a polypeptide encoded by a nucleic acid molecule consisting of a nucleic acid sequence that is degenerate as a result of the genetic code to a nucleic acid molecule as defined in (a) and (b), wherein said antibody binds a phosphorylated epitope.

43. (Currently Amended) [[An]] The antibody according to ~~Claim~~ claim 42 wherein said antibody is a monoclonal antibody.

44. (Currently Amended) [[An]] The antibody according to ~~Claim~~ claim 42 ~~or 43~~ wherein said active binding ~~antibody~~ fragment is a single chain antibody fragment or a domain antibody.

45. (Currently Amended) [[An]] The antibody ~~according to any~~ of ~~Claims~~ claim 42[[-44]] wherein said phosphorylated epitope comprises amino acid residue 671 of the amino acid sequence as shown in SEQ ID NO: 3~~Figure 17c~~.

46. (Currently Amended) [[An]] The antibody ~~according to any~~ of ~~Claims~~ claim 42[[-44]] wherein said phosphorylated epitope comprises amino acid residue 698 of the amino acid sequence shown in SEQ ID NO: 4 ~~Figure 17d~~.

47. (Currently Amended) [[An]] The antibody ~~according to any~~ of ~~Claims~~ claim 42[[-44]] wherein said phosphorylated epitope comprises amino acid residue 746 of the amino acid sequence as shown in SEQ ID NO: 3~~Figure 17c~~.

48. (Currently Amended) [[An]] The antibody ~~according to any~~ of ~~Claims~~ claim 42[[-44]] wherein said phosphorylated epitope comprises amino acid residue 827 of the amino acid sequence shown in SEQ ID NO: 4~~Figure 17d~~.